amount for the treatment of hepatitis in the human of a complex of a cationic liposome with poly(I):poly(C) which has a mean length within the range of 100 to 500 bp.

A marked-up version showing the claim amendments is included in an attachment hereto.

REMARKS

Claims 4 to 11 have been rejected under 35 USC § 103 as allegedly being unpatentable over American Journal of Veterinary Research, Vol. 35, pp. 267-73, 1974 by Wooley et al (Wooley) taken with US 5,298,614 to Yano et al (Yano 1) in further view of EP 0685457A1 to Yano et al (Yano 2).

Applicant respectfully traverses this rejection.

The present invention relates to a method of treating hepatitis in humans. Treatment of hepatitis in mammals is no longer encompassed by the claims.

It is respectfully urged that Wooley does not teach or disclose the instant invention as recited in Claims 4 to 11. Wooley teaches that interferon induced by poly IC shows an effect on canine hepatitis virus. However, the canine hepatitis virus is entirely different from the human hepatitis virus. Applicant urges that the treatment of canine hepatitis virus by poly IC in no way teaches or suggests to the artisan that such treatment would be at all successful in humans.

With all due respect, Applicant urges that the Examiner has incorrectly interpreted the Yano 1 patent disclosure. The Examiner is correct when he acknowledges that Yano 1 teaches that when the chain length is limited to certain ranges, the resulting substance exhibits the desired physiological activity with markedly less toxicity. Yet the Applicant respectfully requests the Examiner refer to column 4 line 35 of Yano 1, which shows that the Yano 1 teaching relates to double stranded nucleic acid derivates and not to double stranded nucleic acids such as poly IC.

The Examiner is also correct insofar as he acknowledges that Yano 1 teaches that the control of molecular size of nucleic acid polymer within a specified range is the primarily important

factor for remarkable reduction of toxicity of poly IC and that the preferred molecular size for using poly IC is from 100 to 600 base numbers. However, Applicant urges that Yano 1 does not teach that conventional poly IC of the short chain length (100 to 600 bp) has strong activity or induces enough interferon. Generally, conventional poly IC alone of the short chain length does not have enough activity or induce enough interferon. With regard to poly IC Yano 1 clarifies that the short chain length reduces toxicity, but in no way clarifies that the short chain length brings enough activity or induces enough interferon. The Examiner is respectfully requested to refer to column 19; wherein Yano 1 merely shows that a double stranded sulphurized nucleic acid derivative of short chain length, poly I: poly ($C_{20}S^4U$), has strong action as an interferon inducer; Yano 1 does not teach or suggest that poly IC of the short chain length has strong action as an interferon inducer.

Applicant urges that the combination of Yano 1 and Yano 2 are initially flawed. Assuming *arguendo* that Yano 2 teaches what the Examiner asserts, it still cannot overcome the deficiencies of Yano 1.

Poly IC alone of the short chain length cannot induce enough interferon to treat hepatitis in humans. Applicant urges that the present inventor's finding that the complex of a catatonic liposome with poly IC of the short chain length could induce enough interferon to treat hepatitis was an unexpected result.

Applicant urges that at the time the invention was made, it would not have been obvious to the skilled artisan. The Examiner is respectfully requested to refer to the experiment shown in Test Example 3 of the present specification. The amount of interferon clinically used on humans is $10^6 - 3 \times 10^6$ IU/person. It has been reported that when β interferon of the 3×10^6 IU/ person was clinically administered to humans, the plasma level of interferon was 67 IU/ml immediately after the administration, and was not detected after 45 minutes. In contrast, when the

complex of the present invention (dose: 100μ g/kg) was administered intravenously to mice, the plasma level of the interferon was 63 IU/ml at 3 hours and was 30 IU/ml as long as 24 hours after the administration. Applicant urges that these unexpected results suggest the great utility of the complex according to the present invention.

Applicant requests reconsideration and withdrawal of this § 103 rejection.

It is believed that all of the present claims are in condition for allowance. Early and favorable action by the Examiner is earnestly solicited.

CONCLUSION

Early and favorable action by the Examiner is earnestly solicited. If the Examiner believes that issues may be resolved by a telephone interview, the Examiner is respectfully urged to telephone the undersigned at (212) 801-2146. The undersigned may also be contacted by e-mail at ecr@gtlaw.com.

AUTHORIZATION

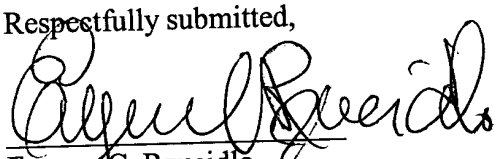
If the Examiner believes that issues may be resolved by telephone interview, the Examiner is respectfully urged to telephone the undersigned at (212) 801-2146. The undersigned may also be contacted by e-mail at ecr@gtlaw.com.

No additional fee is believed to be necessary. The Commissioner is hereby authorized to charge any additional fees which may be required for this amendment, or credit any overpayment to Deposit Account No. 50-1561.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 50-1561.

Respectfully submitted,

Dated: May 5, 2003

By: 

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ATTACHMENT A

4. (Amended) A method of treating hepatitis in a [mammal] human in which interferon is effective, comprising the steps of:

1. intravenously, transmucosally, or hepatic intra-arterially administering to the [mammal] human a complex of a cationic liposome with poly (I):poly (C) which has a mean length within the range of 100 to 500 bp; and

2. inducing chiefly in the liver an effective amount of interferon.

5. (Amended) A method of inducing interferon chiefly in the liver comprising intravenously, transmucossally, or hepatic intra-arterially administering to a [mammal] human an effective amount for the treatment of hepatitis in the [mammal] human of a complex of a cationic liposome with poly(I):poly(C) which has a mean length within the range of 100 to 500 bp.